

REMARKS

Claims 22-42 are pending in this application and under examination. By amendment above, claims 22, 27, 32 and 37 have been amended. No new matter has been introduced into the claims as a result of these amendments. The additional language inserted into claim 22 is supported by language from the preamble of that claim as originally presented. Support for the additional language inserted into each of claims 27 and 32 can be found, for example, in paragraphs [0037] - [0039] and in Example 4 of the application.

Claims 22 and 27 have been rejected under 37 C.F.R. § 112, second paragraph, as being indefinite. Specifically, the examiner asserted that the phrase "other melatoninergic agents" is vague because it was not clear to what other agents the Applicants were referring. Applicants respectfully submit that this rejection has been rendered moot by the amendment above to each of claims 22 and 27 which has deleted this term from the claim. Applicants also have made the same amendment to each of claims 32 and 37.

Claims 22-42 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 6,486,172, issued to Myers et al., and U.S. Patent 6,353,015, issued to Oxenkrug et al. The examiner asserted that the '172 patent teaches that nicotine

increases cognition and attention, citing column 17, lines 30-34, and that the '015 patent teaches that melatonin improves cognition and protects against neurotoxicity, citing column 12, lines 20-25. The examiner further asserted that to use combinations of nicotine and melatonin to treat cognitive and memory impairment would have been obvious because the components are well-known individually for treating those conditions and it would be expected that the combination of components would treat cognition and memory impairment conditions as well. This rejection is traversed.

Submitted with this Amendment is a Declaration Pursuant to 37 C.F.R. § 1.132 by Dr. Moshe Laudon, one of the co-inventors of the invention described and claimed in this patent application. As Dr. Laudon explains, the examiner's position that melatonin is "known to improve cognition and protect against neurotoxicity" is a significant oversimplification of the effects of melatonin administration to humans. The effects of melatonin administration can vary significantly depending on such factors as the time of day at which it is administered, the amount administered and the identity of any other pharmacological agents that the patient is taking. A review of the literature on melatonin administration shows that the effects of melatonin on cognition, memory and/or sleep are unpredictable: sometimes it

appears to be useful, as in the reference cited by the examiner, in other instances it either has no effect or it impairs cognition, memory and/or sleep. Dr. Laudon cites one reference in which the administration of melatonin appeared to have no effects on cognition or memory and a number of references in which melatonin administration impaired cognition and memory.

As the detailed discussion in Dr. Laudon's declaration shows, it is highly inaccurate to assert, on the basis of the statements in the Oxenkrug et al. patent, that melatonin "improves cognition." All that can be learned from the Oxenkrug et al. patent is that administration of melatonin showed cognition-enhancing and neuroprotective properties in animal and cell models of Alzheimer's Disease-type neurodegeneration. This limited conclusion is, in fact, that of the patentees, and the limited testing that they reported does not provide a basis for a reasonable belief that the administration of melatonin will improve sleep quality, cognition or memory in persons undergoing nicotine replacement therapy, especially in view of the numerous examples in the literature that melatonin administration can decrease cognition and memory.

The limited conclusion that properly can be drawn from the Oxenkrug reference, taken in combination with the teachings of the Myers reference is wholly insufficient to render obvious the

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present invention. A person of skill in the art who read each of these references would have no inclination to consider the teachings of the two references in combination, and even if he were to do so, he would not be lead to the present invention.

In view of the foregoing amendments, discussion and accompanying declaration, Applicants respectfully submit that the claims under examination are in condition for allowance.

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